Remarks

Claims 21, 23-25, and 27-52 are pending in the subject application and currently before the Examiner (with claims 35-50 standing withdrawn from consideration as being directed to a non-elected invention). Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants gratefully acknowledge the Examiner's withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, and the "obviousness-type" double patenting rejection.

Claims 21, 23-25, 27-34, 51, and 52 are rejected under 35 U.S.C. § 103(a) as obvious over Belmant *et al.* (WO 00/12516 and U.S. Patent No. 6,660,723), in view of Garcia *et al.* (1998) and Valeri (1976). Claims 21, 23-25, 27-34, 51, and 52 are also rejected under 35 U.S.C. § 103(a) as obvious over Espinosa *et al.* (2001) in view of Garcia *et al.* (1998) and Valeri (1976).

As discussed previously, Applicants respectfully submit that the presently claimed method produces unexpected results as compared to methods similar to those of Espinosa *et al.* and Belmant *et al.* For example, culture of biological preparations as defined and according to the claimed methods where the cell density was maintained at less than about 5×10^6 cells/ml during the culturing step resulted in the generation of cell preparations containing greater than about 90% gamma delta T lymphocytes after 10 days of culture, greater than about 95% gamma delta T lymphocytes after about 15 days of culture and about 95% gamma delta T lymphocytes after 21 days of culture (see paragraph bridging pages 25-26 and Table 8). These results were reproducible and consistent across multiple samples. In contrast, Espinosa *et al.* teach that their method resulted in producing, maximally, a population of gamma delta T-cells that was about 60% of the total T-cells in culture (see Figure 4B) and Belmant *et al.* provides no apparent teaching as to the number of cells at which the culture is to be maintained nor does the reference provide any expectation that one would be able to provide a gamma delta T-cell population that is as enriched as is that provided by the claimed invention. Accordingly, it is respectfully submitted that the claimed method is not obvious over the teachings of the cited references as it produces unexpected results as compared to the results from following a protocol substantially similar to that of Belmant *et al.* or Espinosa *et al.*; namely, the claimed method reproducibly produces gamma delta T lymphocyte populations that contain significantly more gamma delta T lymphocytes as compared to the cited prior art methods. In view

of such unexpected results, reconsideration and withdrawal of the rejections is respectfully requested.

Applicants also submit that a longer culture period would not ensure a higher number and percentage of γδT lymphocytes. Indeed, there are two steps during the culture, an amplification step, and then, a differentiation step from naïve to effector cells. During the differentiation step, cell proliferation drastically slows down; therefore, there is no correlation between number and percentage of γδT lymphocytes and the length of the culture period. Similarly, the cell density is an important aspect to achieve the seeking result. Indeed, still contrary to what has been in the Office Actions, a higher density would not be successful to reach a higher number and percentage of γδT lymphocytes because it would lead to death of the majority of the cells.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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